



Novel Microbiome Applications Infiltrate the Cancer Space

Microbiome research has come from behind the scenes to take center stage in the behemoth cancer research space. At Kisaco Research's [Cancer Microbiome Congress](#), on May 8th-9th 2018 in Boston, we'll hear insight on cutting edge developments in this newly evolving field, and we'll have the opportunity to network with international representatives from biopharma, academia, biotech and microbiome-focused companies. Novel breakthroughs and insights in this space will be presented by the Mayo Clinic, MD Anderson, NIH, Johns Hopkins, MIT, Merck, Seres Therapeutics, Vedanta, CosmosID, Enterome, as well as others. The two-day conference will explore microbiome applications from different angles: cancer initiation and progression, microbial therapeutics, drug response, and a role in diagnostics and prevention. Here is a snapshot of what to expect.

Deep Microbiome Exploration for Early Diagnosis and Cancer Progression

Marina Walther-Antonio, Assistant Professor of Surgery at the Mayo Clinic, captures microbiome signatures to improve early diagnosis of uterine & cervical cancers. By sifting through benign endometrial biopsies, she looks for patterns in the biopsy microbiome that can stratify patients by predicted treatment outcome, which could ultimately provide early treatment with the optimal therapy. She is also exploring ovarian cancer microbiome signatures for their potential in early diagnosis as well as the impact of microbiota on ovarian cancer recurrence. By closely examining microbiome signatures in patients with endometrial cancer through host-microbial tissue culture studies, the role that these bacteria play in cancer can be elucidated. At the conference, Walther-Antonio will explore some of these topics and discuss the potential for the microbiome to be used as a drug target.

We'll hear from Manoj Dadlani, CEO of CosmosID about how changes in the microbial community and/or specific microbes are associated with gastric, lung, oral, pancreatic, or cervical cancers. CosmosID offers whole-genome shotgun metagenomics, which captures the sequence of every microorganism's entire genome in a sample, helping researchers identify and characterize potential functions for all microorganisms (including bacteria, viruses, fungi, and parasites) present in a sample. A key feature is that this platform provides critical accuracy at the strain level, which is important for R&D and modification of the microbiome. CosmosID is participating in the National Cancer Moonshot, a White House initiative to accelerate the prevention, diagnose, and treatment of cancer.

Exciting, Diverse Approaches to Microbial Therapeutics

An interesting aspect of tumors is that they outgrow their blood supply, leading to a hypoxic, immune-privileged environment in the tumor environment. This hypoxic environment reduces the effectiveness of chemotherapy and radiation. A promising anticancer agent, a non-toxic strain of the anaerobic bacterium *Clostridium novyi*, can exploit this hypoxic and immune-privileged environment. This bacteria can be injected intravenously, find its way to tumors, colonize them, and cause them to die off or regress. To add insult to injury against the tumor, a *C. novyi-NT* infection also instigates a host antitumor immune response, critical for preventing tumor recurrence. A third notch in its belt is the bacterium's propensity for enhancing the effectiveness of other cancer therapeutics and lastly, it can even operate as a tumor-specific gene therapy vector. We will hear from Shibin Zhou of Johns Hopkins University School of Medicine on these exciting topics.

Vedanta Biosciences is taking another approach, developing consortium of bacteria to stimulate immunoregulatory responses for treatment of allergic and autoimmune diseases, as well as bacterial consortium that are conducive to immunopotentiating responses for cancer and vaccination. One of Vedanta Bioscience's products is VE800, in development for cancer immunotherapy. Bruce Roberts, CSO of Vedanta Biosciences, will share their progress in using metagenomics & Next-Gen sequencing to create rationally selected consortia, as well as their methods for exploring inter-microbial interactions to determine mechanisms of action.

Groundbreaking Insight into the Role of the Microbiome and Immunotherapy Response

In a landmark [Science article](#) (Nov. 2017), Vancheswaran Gopalakrishnan of the Wargo Lab at MD Anderson produced the first well-characterized study in human cancer patients showing the distinct differences in gut microbiomes in immunotherapy responders versus non-responders. Melanoma cancer patients that were responders to anti-PD-1 immunotherapy had a significantly different gut microbiome composition and diversity of *Ruminococcaceae* bacteria as compared to patients who were non-responders. Gopalakrishnan and team used both metagenomics analysis and immune profiling, and found that the microbiome of the responding patients provided their host with an enhanced systemic immunity in addition to anti-tumor immunity. Gopalakrishnan will share a case study on predicting responders versus non-responders for patients considering treatment, the next steps needed to improve checkpoint inhibitor immunotherapy, and the exciting possibility of manipulating and optimizing the microbiome before immunotherapy to improve anti-PD1 efficacy.

This exciting research developed at MD Anderson is already moving into clinical trials in a collaboration with Seres Therapeutics and the Parker Institute for Cancer Immunotherapy. A randomized, placebo-controlled clinical study in patients with advanced metastatic melanoma will be conducted using Seres Therapeutics' oral microbiome therapy SER-401, which is a live bacterial consortium designed specifically to enhance the safety and efficacy of immunotherapy treatment. We'll hear more on this clinical study from David Cook, Executive VP of R&D and CSO of Seres Therapeutics.

Emulate – a spin-out of Harvard’s Wyss Institute – has developed a 3D intestine-on-a-chip, which may have potential applications in studying microbiome-host interactions and drug response. One benefit is the move away from animal testing, which is expensive and has the drawback of not always capturing toxic side effects. Emulate also has lung, liver, and skin chips, all of which are packed with cells to resemble human organs on small translucent chips similar in size to USB-drives. Emulate analyzes these with their companion software and instrumentation. By using a patient’s own stem cells to reproduce the intestinal lining on their intestine-on-chip, multiple drugs can be tested in a precision medicine approach, preventing expensive, ineffective exposure to drug treatments with potentially harmful side effects. The best drug for the patient can then be used therapeutically. We will hear from Dr. Jordan Kerns, Senior Scientist at Emulate, about the challenges, applications and advantages of their intestine-on-a-chip for microbiome studies, and how it can be used to complement animal studies.

Diagnostics and Prevention

MIT’s Dr. Susan Erdman brings us her insight into the inter-connection between gut bacteria, the immune system and cancer. Her research provides evidence that early life bacterial infections enhance functions that inhibit disease processes later in life. For example, regulatory T_{REG} cells (a key player in preventing autoimmune diseases by maintaining self-tolerance) were shown to inhibit disease (non-B non-T cell-mediated colitis) after prior exposure to pathogenic *Helicobacter hepaticus* bacteria. Their research supports the paradoxical ‘hygiene hypothesis’, in which developed countries and more recently developing countries have a higher incidence of allergic and autoimmune disease due to a lower risk of early life infection. To protect against inflammation-associated pathology, a targeted treatment with bacteria may be warranted. This means we need to transition from our deeply embedded sense that pathogenic bacterial are always harmful, as they may at times benefit our long term health by reducing chronic autoimmune disease and cancer. We’ll hear more about Erdman’s research which provides evidence of this.

These topics and much more will be presented at the 2018 Cancer Microbiome Congress. Hope to see you there!

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